A Search for a Threshold in the Relationship of Air Pollution to Mortality: A Reanalysis of Data on London Winters

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The relationship between air pollution and increased risk of mortality has been explored previously using data on 14 winters in London. The results of these analyses have been used to determine a no-observable-effects level. This reanalysis of the data finds no evidence to support the existence of a no-effects level. Further, the reanalysis suggests that the estimated pollution-mortality relationship exists even in nonepisodic winters, when British Smoke readings were less than 500 $\mu g/m^3$.

As part of its scientific review for determination of the National Ambient Air Quality Standard for particulate matter, the U. S. Environmental Protection Agency (USEPA) has been re-evaluating the analyses of the London winters of 1958–59 through 1971–1972. Unfortunately, the original research by Martin and Bradley (1,2) and a subsequent effort by Mazumdar et al. (3) have left unaddressed many important issues regarding the relationship of air pollution to increased risk of mortality. This note addresses two major uncertainties that have surfaced in USEPA publications (4) and in public comment regarding the analysis of the London data.

The first uncertainty concerns the determination of a no-observed-effects level (NOEL). In attempting to determine a NOEL, USEPA's Office of Research and Development used an exposure–response relationship estimated by Mazumdar et al. (3) to suggest a "more marked" risk to mortality in the 500 to 1000 $\mu g/m^3$ range for British Smoke (BS),† with a smaller risk in the 150 to 500 $\mu g/m^3$ range (4). (This description of the relative risk is an obvious result of the assumed quadratic form which has a greater slope at higher BS levels.) In addition, research on bronchitics by Lawther (5) was cited as evidence of effects at BS = 250$\mu g/m^3$. From these studies, BS = 150 $\mu g/m^3$ was determined to be the threshold for an "effects possible" level.

Unfortunately, the NOEL issue was not resolved in the hearings conducted by USEPA's Clean Air Scientific Advisory Committee (CASAC), in the Criteria Document, or in the studies of Martin and Bradley (1,2) or Mazumdar (3). In their assessment of these studies, Ware et al. (6) suggested that the evidence of effects at low levels was inconclusive.

Analysis (1–3) indicated that both linear and quadratic models fit the 1958–1972 data equally well. The linear model suggests a higher risk at low BS levels than does the quadratic model. However, neither the linear nor the quadratic model support the existence of a NOEL. By definition, both functional forms indicate a BS coefficient significantly different from zero over its entire range. While statistical tests of the data cannot prove conclusively whether or not a NOEL exists, they can indicate whether the data are consistent with the assumption of a NOEL at a certain level. Such a technique will be employed in this note to address the first uncertainty concerning the existence of a NOEL at BS = 150 $\mu g/m^3$.

The second uncertainty concerns the representativeness of the 1958–59 winter used in the 1960 paper (1) in establishing an air pollution–mortality relationship. The average BS level that winter was 551 $\mu g/m^3$, and inferences based on these levels may be questionable at today's ambient levels. In subsequent years, however, BS fell almost monotonically, reaching average values in the 60 $\mu g/m^3$ range in the late 1960s and early 1970s.

To address the concern about the representative nature of the 1958–59 winter, the analysis incorporates the last seven winters (1965–66 to 1971–72) of the 14 winters of data. Not only does this test the stability of the model, it enables one to test the mortality–BS relationship in years in which there were no episodes (BS values above 500 $\mu g/m^3$).

Since CASAC has accepted both the data and methodology employed previously (1–3) as a reasonable basis for

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†British Smoke is a measure of pollution closely related to the measure of particulate matter in the United States.

standard setting, a generally similar methodology is adopted here. CASAC has also determined that the differences in particle size, chemical composition, and measurement technique for BS versus total suspended particulates do not preclude the use of the London data for establishing U.S. particle standards. The high degree of collinearity between BS and sulfur dioxide observed during London winters precludes an accurate analysis of the separate impacts of these pollutants on mortality. Inclusion of both of these variables in a regression would tend to result in an overestimation of their variance. Since evidence exists that particles may have the greater impact on health, only BS is included in the subsequent regression analysis, as a measure of the total air pollution insult. The existence of health effects from exposure to SO_2, however, cannot be ruled out.

Testing for a No-Effects Level

To test specifically for the existence of a NOEL, a simple variation of a standard multiple regression model was used (7,8). In this model, the investigator can test whether the data support the existence of a given pollution level as a NOEL.

The observations of the pollution levels were divided into two segments, depending on whether they fall below or above the hypothesized NOEL of BS = 150. If a statistically significant t value for the estimated slope coefficient is observed for the lower level of pollution, one can reject the hypothesis of "no effect." The regression analysis would then indicate that at the lower level, a statistically determined relationship exists between pollution and mortality. In the opposite case, when the t value for the lower level of pollution is not significant, one would accept the hypothesis that the slope is zero. This would support the conclusion that a NOEL exists.

A number of different specifications for the air pollution–mortality relationship in London winters have already been estimated. Martin and Bradley (1) simply regressed deviations in daily mortality from a 15-day moving average on BS alone. This use of deviations

helps control for omitted variables and the potential influence of slow-moving epidemics. Mazumdar et al. (3) used a more complex model that attempted to net out the influence of temperature and humidity, in order to isolate air pollution impacts.

To control for the influence of weather factors and test for the existence of a threshold level, a regression of the form (1) is used:

$$DM_t = a_0 + a_1 B_{1t} + a_2 B_{2t} + a_3 T_t + a_4 H_t \qquad (1)$$

where DM = deviations in daily mortality from a 15-day moving average; B^* = hypothesized NOEL; B_1 = British Smoke (BS) for BS $\leq B^*$, and = B^* for BS > B^*; B_2 = BS - B^* for BS > B^*, and = 0 otherwise; T = daily average temperature; H = relative humidity; t = day of the winter. A NOEL level of BS-150 $\mu g/m^3$ was hypothesized. Particular attention was given to the London winters of 1965-66 through 1971-72, to eliminate the possibility of an extreme episode (BS > 500 $\mu g/m^3$) affecting the results.

The results, testing for an assumed NOEL of 150 BS, are presented in Table 1. The analysis indicated that there is consistently a statistically significant pollution effect on mortality below the BS = 150 level. For 11 of the 14 winters, the coefficient of B_1—the values below 150 BS—was statistically different from zero at the 0.10 level or better. (Since we wanted to test whether BS was positive and significant, a one-tailed test was used. The t values corresponding to 0.10, 0.05, and 0.01 levels are 1.28, 1.65, and 1.96, respectively.) In nine of the years, the coefficient of B_1 is significant at the 0.05 levels while in eight of the years it is significant at the 0.01 level.

Focusing on the last seven winters, starting in 1965-66 when there were no BS values above 500 $\mu g/m^3$, B_1 is significant at the 0.05 level in six years and at the 0.01 level in four of the years. These results indicate a strong association of BS with mortality, holding temperature and humidity constant, at levels below 150 BS.

The analysis also indicated a lower estimated coefficient for values in the upper range of BS. For a number of reasons this result should not necessarily be considered

Table 1. Exploring a possible threshold.

| Winter | British Smoke (BS) values, $\mu g/m^3$ | | | Low BS | | High BS | |
	Minimum	Mean	Maximum	B_1	(t value)	B_2	(t value)
1958–59	133	552	1965	− 0.273	(0.252)	0.050	(7.72)
1959–60	122	353	1433	− 0.468	(0.735)	0.029	(3.02)
1960–61	81	255	754	0.311	(1.91)	0.043	(3.80)
1961–62	42	198	793	0.153	(2.21)	0.052	(3.00)
1962–63	18	208	1971	0.048	(0.606)	0.076	(6.10)
1963–64	22	191	734	0.082	(1.33)	0.052	(3.02)
1964–65	27	132	660	0.125	(2.10)	0.038	(1.41)
1965–66	15	107	397	0.142	(2.85)	0.05	(1.16)
1966–67	22	98	405	0.144	(3.01)	0.055	(1.10)
1967–68	12	83	317	0.130	(2.17)	− 0.008	(0.075)
1968–69	11	66	211	0.191	(3.85)	− 0.110	(0.518)
1969–70	19	73	335	0.149	(2.30)	0.049	(0.462)
1970–71	16	67	258	0.088	(2.02)	0.055	(0.527)
1971–72	19	60	226	0.091	(1.54)	0.430	(1.85)

as problematic. First, as indicated earlier, over time there are fewer observations in the upper range, and an effect simply may be harder to discern. Second, after considering the variance of the coefficients of B_1 and B_2, it is possible that the slopes are not significantly different. Third, because of the potential of larger proportional measurement error as BS increases, it is possible that downward bias may increase with larger BS values. Fourth, the pattern may simply be a fit of the S-shaped dose–response curve. Fifth, it is possible that deviations in mortality (as opposed to crude mortality) simply respond more to lower pollution levels in nonepisodic years. Sixth, the result may be due simply to the 150 BS cut point chosen for the model. Seventh, lower measured levels of BS may contain a higher proportion of the more toxic constituents such as sulfuric acid or of the smaller particles that may actually penetrate the pulmonary region. Finally, there may be interactive effects associated with weather.

In sum, the results of this analysis for the nonepisodic winters of 1965–66 through 1971–72 indicate that the statistically significant relationship between BS and deviations in daily mortality is not due to the high end values of an atypical winter (1958–59). Rather, this analysis of the data suggests that the lower values of BS are associated significantly with deviations in mortality in years when there are no BS values above 500 $\mu g/m^3$. Further, for the data set as a whole, there is no evidence to support a no-observed-effects level at BS = 150 $\mu g/m^3$.

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